## REMARKS

Claims 22, 30, 32, 41-42, 45, 48-49, 58-66 are pending. Claims 24, 25-29, 33, 35-40, 50, 52-57 have been cancelled as drawn to non-elected inventions. Claims 43, 44, 46, and 47 have been cancelled without prejudice or disclaimer; Applicants reserve the right to pursue claims of similar scope in related applications. Claims 23, 34 and 51 have been cancelled because election of Group I required amending independent claims 22, 30 and 42 to disclose a caspase. Cancellation of the claims does not affect inventorship. Support for new claims 59-66 derives from the specification and claims as originally filed. For example, caspases and the selection of appropriate substrates is described in the specification at pages 22-23. Accordingly, the amendments do not present new matter and entry is proper.

**Recordation of Telephone Interview held on May 6, 2004**

Applicants discussed the Restriction Requirement applied to pending claims 22-58. In particular, Applicants discussed the appropriateness of applying a restriction requirement when pending claims 22-58 had been examined in three non-final office actions. Thus, it was Applicants position that the burden on the Examiner as set forth in MPEP § 803 was not serious. In support of their position, Applicants pointed out that under MPEP § 808.02, the Examiner had not demonstrated a separate classification, a separate status in the art, or a different field of search.

The Examiner's position was that the thrust of the pending claims 22-58 was drastically different from what was originally filed. Thus, the Examiner was required to research the claims over and over again, which was burdensome, and, hence the restriction requirement was proper.

Applicants then pointed out if the restriction requirement was not withdrawn, that the inventions classified under Group I, Group II, V, and VI should be classified in the same Group, as the cysteine proteases (i.e., Group III), because caspases, interleukin-1-beta converting enzyme, calpain and cathepsins are all cysteine proteases.

The Examiner position is that for each protease a separate search of the art would be required because their cleavage sites and peptide interactions would be different, and thus, the restriction requirement was proper.

In conclusion, no agreement regarding the appropriateness of the restriction requirement and the classification of the inventions disclosed in pending claims 22-58 was reached.

**Sequence Listing**

The amendments are made in adherence with 37 C.F.R. § 1.821-1.825. This amendment is accompanied by a floppy disc containing the above named sequences, SEQUENCE ID NUMBERS 1-8, in computer readable form, and a paper copy of the sequence information.

The information contained in the computer readable disc is identical to that of the paper copy in adherence with 37 C.F.R. § 1.821(f). This amendment contains no new matter in adherence with 37 C.F.R. § 1.821(g). Applicant submits that this amendment, the accompanying computer readable sequence listing, and the paper copy thereof serve to place this application in a condition of adherence to the rules 37 C.F.R. § 1.821-1.825.

**Restriction Requirement**

The Examiner requires Applicants to elect one of the following groups of inventions:

Group I (*Claims 22, 23, 30, 32, 33, 34, 41-51, and 58*) drawn to a MRI composition and use thereof wherein the protease is a caspase, classified in class 424, subclass 9.3;

Group II (*Claims 22, 24, 30, 32, 33, 35, 41-50, 52, and 58*) drawn to a MRI composition and use thereof wherein the protease is a interleukin- 1 beta-converting enzyme, classified in class 424, subclass 9.3;

Group III (*Claims 22, 25, 30, 32, 33, 36, 41-50, 53, and 58*) drawn to a MRI composition and use thereof wherein the protease is a cysteine, classified in class 424, subclass 9.3;

Group IV (*Claims 22, 26, 30, 32, 33, 37, 41-50, 54, and 58*) drawn to a MRI composition and use thereof wherein the protease is a serine, classified in class 424, subclass 9.3;

Group V (*Claims 22, 27, 30, 32, 33, 38, 41-50, 55, and 58*) drawn to a MRI composition and use thereof wherein the protease is a calpain, classified in class 424, subclass 9.3;

Group VI (*Claims 22, 28, 30, 32, 33, 39, 41-50, 56, and 58*) drawn to a MRI composition and use thereof wherein the protease is a cathepsin, classified in class 424, subclass 9.3; and

Group VII (*Claims 22, 29, 30, 32, 33, 40, 41-50, 57 and 58*) drawn to a MRI composition and use thereof wherein the protease is a metalloproteinase, classified in class 424, subclass 9.3; and,

Group VIII (*Claims 22, 30, 32, 33, 41-50 and 58*) drawn to a MRI composition an duse thereof wherein the protease is not one from Groups I-VIII above, classified in class 424, subclass 9.3.

As a preliminary matter, Applicants wish to point out that the peptide substrate for cysteine proteases does not comprise a cysteine residue (see Restriction Requirement, page 3). Rather, the presence of a cysteine residue in the active site of a protease is used to classify the protease as a cysteine protease.

Applicants elect Group I, claims 22, 23, 30, 32, 33, 34, 41-51, and 58 drawn to a MRI composition and use thereof wherein the protease is a caspase, with traverse.

Applicants respectfully traverse the Examiner's Restriction Requirement for the following reasons. Applicants respectfully submit that the caspases, currently classified in Group I, and interleukin-1-beta-converting enzyme (ICE), currently classified in Group II, should be classified in the same restriction Group. Applicants respectfully point out that ICE is alternate name for caspase-1. In support of Applicants position, Applicants enclose the following papers:

1. Zhivotovsky, et al., 1996, Experientia, 52:968-978 (i.e. Exhibit 1);

2. Cohen, G., 1997, Biochem. J., 326: 1-16 (Exhibit 2);

3. Thornberry, N.A., 1996, British Medical Bulletin, 53: 478-490 (Exhibit 3); and,

4. Solary, et al., 1998, Cell Biology and Toxicology, 14:121-132 (Exhibit 4).

As set forth in the above papers, the caspase family of proteases includes ICE.

In addition, the Applicants respectfully submit that inventions I and II are clearly related, as they disclose members of the caspase family of proteases. Accordingly, Applicants respectfully request that the Examiner examine Inventions I and II together on the merits.

**Election of Species Requirement**

Applicants are required to elect a single peptide sequence compatible with the protease selected from the group above. Applicants elect the sequence Tyr-Val-Ala-Asp-Ala-Pro-Val, which is a peptide substrate know to be cleaved by caspase-1.

Claims 22, 30, 32, 41-42, 45, 48-49, and 58-66 read on the elected species.

This election is made without traverse with the understanding that should allowable subject matter be found, Applicants are entitled to consideration of a generic claim encompassing additional species, such as those disclosed in claims 22, 30, 32, 41-42, 45, 48-49, and 58-66. *See* M.P.E.P. § 806.04(d).

Please direct any calls in connection with this application to the undersigned at (415) 781-1989.

Respectfully submitted,

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Dated: 5/19/04

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